UNITED STATES DISTRICT COURT OF THE SOUTHERN DISTRICT OF WEST VIRGINIA CHARLESTON DIVISION

IN RE: DIGITEK PRODUCT LIABILITY LITIGATION

MDL Case No.: 2:08-md-1968

THIS DOCUMENT RELATES TO:

McCornack v. Actavis, 09-cv-0671
Vega v. Actavis, 09-cv-0768

PLAINTIFFS' OPPOSITION TO DEFENDANTS' MOTION FOR SUMMARY JUDGMENT (Pacer Docket Nos : 523-524).

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I. INTRODUCTION

Plaintiffs respectfully submit these points and authorities in opposition to defendants' motion for summary judgment in MDL No. 1968, (Doc. Nos. 523-524). Contrary to Defendants' bombastic arguments, there is ample evidence that defective, excess-strength Digitek reached the marketplace and were consumed by Plaintiffs. The recall of Digitek came 5 weeks after Dan McCornack died of Digoxin Toxicity.

II. STATEMENT OF FACTS

A. Actavis' Discovery of Double-Thick Digitek: On November 30, 2007 (four months prior to Mr. McCornack's death), packaging of 0.125 mg Digitek batch no.70924A1 was halted after a worker found two double-thick tablets in the hopper (bucket nos. 15 and 16). Pl. Ex. 44; Pl. Ex. 16, (Bates 2, 4); Pl. Ex. 500, (Bates 678, ¶39, A31-32). Half of the 4.7 million tablet batch (bucket nos. 1-14) had already been packaged for distribution. The ensuing FDA investigation led to a recall of all Digitek (and certain other Actavis' products), and ultimately the recall of all products produced at the Little Falls facility. *See, II.D, below*.

Visual inspection of the two buckets in the hopper (nos. 15-16) and the two subsequent buckets (nos. 17 and 18) was conducted, finding a third defective double-thick tablet in bucket 17. The remainder of the unpackaged portion of the batch (bucket nos. 19-34) was visually "inspected" by keeping a "watchful eye" ***as the tablets traveled down the bottle filler channels***.[1]

[1] A single batch of Digitek, comprising approximately 4.8 million pills, is typically manufactured and packaged in just a few days. Even assuming 24-hour per day packaging, this would still be more than one thousand pills per minute traveling down the bottle filler channels.

Pl. Ex. 44, Pl. Ex. 16, (Bates 4); Pl. Ex. 500, (Bates 678, ¶39 and A31-32). A fourth and fifth defective double-thick tablet were found in bucket no. 34. Pl. Ex. 16, (Bates 4).

Later, the 4,772 packaged 1,000 tablet bottles comprising the batch were emptied onto a table-top, and visually "inspected." Actavis discovered 15 more double-thick tablets. Pl. Ex. 16, (Bates 55-56, 61). Finally, Actavis visually inspected 1,330 tablets (40 tablets from each full bucket, 10 from the partially-filled bucket). Pl. Ex. 16, (Bates 61-63). In total, 20 defective, double-thick tablets were found, scattered randomly throughout the 4.7 million tablet batch.

At all stages, this "inspection" was limited to a naked-eye, visual scanning of the tablets. *See citations supra*. The defects at issue, however, offer minimal or no visual cues to ensure the efficacy of such a cursory visual inspection. Defendants themselves argue that a double-thick tablet cannot reliably be detected by eye. *Doc. No. 527*, p. 1, ("Thickness of a tablet only millimeters in size is a measurement. It is not something that can be 'eyeballed.'"). Related excess-weight and blending defects (*see, II.B, below*) would have no visual cues whatsoever.

Actavis admitted that it could not confirm any cause for these defective double-thick tablets, speculating that it might have resulted from a mid-batch stop and re-start of one (of two) tablet press. Pl. Ex. 16, (Bates 6). Other records, however, suggest that the tablet press itself may have been defective. Pl. Ex 97; Pl. Ex. 227.[2] Either way, Actavis chose to treat this as an "isolated incident", concluded no other batches were impacted, and quickly released the repackaged batch for distribution. Pl. Ex.16, (Bates 5-7).

B. Actavis' History of Related Production Deficiencies: Actavis (and its predecessor, Amide, with the same facilities and management from 1989-2008), has a decades-long history of serious production deficiencies. The FDA has issued Actavis no less than 26

[2] Replacing the Digitek tablet presses has actually been a longstanding topic of discussion at Actavis. *See also, e.g.*, Pl. Ex. 258, Pl. Ex. 259.

Form 483's (most documenting numerous quality control deficiencies) and 6 warning letters highlighting "significant deviations" from Current Good Manufacturing Practice ("cGMP") regulations (21 *C.F.R.* Parts 210 and 211). Pl. Ex. 500, *generally*. Between 1990 and 2008, Actavis' products were the subject of four separate recalls, three related to incorrect tablet thickness, weight, or blending, (*i.e.*, excess or insufficient dosage). The last of these recalled every single Actavis product produced at its Little Falls facility. Pl. Ex. 500, *and II.D, below*. For much of this time, (from 1992-2002, and 2008 forward), Actavis has operated under the terms of a consent decree because the company was deemed incapable of safely operating its facilities without third-party oversight. Pl. Ex. 500, (A3, A47, B45).

The full history of Actavis' documented failure to ensure that products were produced within specifications is succinctly summarized in Dr. David M. Bliesner's expert report (Pl. Ex. 500, with repeated instances of incorrect tablet thickness, weight, and/or blending, including product packaged for shipment or found in the marketplace. *Inter alia*:

- In December 1990, Actavis initiates a Class II recall for variation in tablet size resulting in sub- and super-potent product. Pl. Ex. M45; Pl. Ex. 500, (B5, A33).

- In March 1994, the FDA documents loss of active ingredient during drying and final blending/compression without concern or explanation by Actavis. Pl. Ex. 500, (A4).

- In October-November 2001, the FDA finds "thin" (*i.e.*, sub-strength) tablets, rejecting more than 1,600 tablets during a visual inspection, and no assurance that all defective tablets had been found. Pl. Ex. 236; Pl. Ex. 500, (A11).

- On June 8, 2004, a double-thick/double-weight 0.25 mg digoxin tablet from a batch produced seven months prior (November 2003) with tablet presses #67 and 71 is found by a pharmacist. Pl. Exs. 241, 242, 128; Pl. Ex. 500, (A13-A15).

- In July-August 2006, the FDA concludes that Actavis has failed to document all laboratory and manufacturing deviations. Pl. Ex. 90; Pl. Ex. 500, (A18).

- In the first half of 2007, 19 product batches have blend uniformity failures, including two batches of digoxin. One of these two is released. Pl. Ex. 183.

- On April 3, 2007, Actavis confirms 17 Adverse Drug Events (including elevated digoxin blood levels and an "unknown" potency question) and blend uniformity defects (particularly with respect to batch no. 60319A) relating to the 184 million 0.25 mg digoxin tablets produced in 2006 (44 batches). Pl. Ex. 253; Pl. Ex. 500, (A27).

- On May 22, 2007, Actavis reports out-of-specification digoxin tablets (weight) in batch no. 5453A (produced in 2005). Pl. Ex. 500, (A26); Pl. Ex. 501.

- On November 30, 2007, 20 defective double-thick 0.125 mg digoxin tablets are fortuitously discovered during packaging, scattered throughout digoxin batch no. 70924A1, produced with tablet presses #67 and 71. Following a cursory visual inspection, the product is released to market anyways. Pl. Exs. 44, 16; Pl. Ex. 500, (A31-32), *and see, II.A, supra*.

- In late 2007, Actavis speculates a blend failure with respect to digoxin batch nos. 70148A and 70207A could have had various causes, including dry (low humidity) winter conditions during winter and API particle size variations. Pl. Ex. 159; Pl. Ex. 500, (A34).

- In January 2008, Mylan (a Digitek distributor), confirms two batches of 0.125 mg Digitek with out-of-specification assays (too low). Pl. Ex. M14; Pl. Ex. 500, (A52).

- On February 20, 2008, Actavis' discovers sub-thickness 0.25 mg Digitek tablets in bucket no. 2 of batch no. 80133A. Pl. Ex. 217, (Bates 515); Pl. Ex. 500, (A54).

- In March 2008, UDL, another Digitek distributor, notes the complaint of a consumer who received sub-thickness tablets. Pl. Ex. M69; Pl. Ex. 500, (A36).

- On April 1, 2008, packaged overweight 0.125 mg Digitek is discovered near the end of packaging batch no. 80228A1, (bucket nos. 26 and 27). In one 5,000 pill bottle, 17 out of 30 pills inspected are of excess weight, and 17 out of 50 tablets are in excess of 120 mg, (10-20% above weight specifications). Pl. Ex. 141; Pl. Ex. 500, (A39); Pl. Ex. 16, (Bates 4).

- From March-May 2008, the FDA inspects Actavis due to the "significant cGMP deficiencies" relating to double-thick tablets and blend failures, ultimately prompting the Digitek recall. *See, II.C-D, below*.

- On April 24, 2008, one month after Mr. McCornack's death, all Digitek is recalled due to double-thickness, overweight, excess-strength tablets. Certain other Actavis products are also recalled and production of all drugs is suspended. *See, II.C-D, below*; Pl. Ex. 113; Pl. Ex. 500, (A35); Pl. Ex. 502, (Bates 782-83).

- In late April 2008, just days after the recall, a Digitek tablet "obviously of double thickness" is discovered at a Massachusetts nursing facility. Doc. No. 527-1, (Page ID# 12224); Pl. Ex. 621.

- In August 2008, Actavis recalls all 66 products manufactured at its Little Falls facility. Pl. Ex. 500, (B43).

- Actavis' rejects 8 of 19 batches of 0.125 mg Digitek produced in early 2008 (after the November 2007 incident) in connection with the recall, including one with tablets out-of-specification for weight. Pl. Ex. 144, (Bates 357-358 and n. 4); Pl. Ex. 500, (A48).

- In January 2009, Actavis reports nine complaints (from Aug.2008- Jan. 2009) of double-thick Digitek found in the marketplace. Pl. Ex. 73.

Dr. Bliesner, a respected expert concerning Current Good Manufacturing Practice ("CGMP") and Quality Safety Regulations compliance for the pharmaceutical industry, reviewed the foregoing history (and numerous other similar reports). He concludes that Actavis (and its predecessor) have a documented, 27-year failure to comply with cGMP's. He further concludes that the systemic failure to implement quality control systems and to comply with applicable safety regulations resulted in adulterated Digitek with double-thick/double-weight/excess strength reaching the marketplace. Pl. Ex. 500, (Bates 683); Pl. Ex. 620. His conclusions are echoed by no less than three other respected pharmaceutical industry and compliance experts. *See, e.g.*, Pl. Ex. 511; Pl. Ex. 514; Pl. Ex. 513, (450:25-454:6, 411:9-24); Pl. Ex. 516.

C. The FDA's March - May 2008 Investigation: From March –May 2008, the FDA inspected Actavis' Riverview, New Jersey facilities (the new site for the former Little Falls facility's operations). The FDA succinctly describes its longstanding concerns:

> … significant cGMP deficiencies including but not limited to out of specification in-process, finished product and stability results for more than [redacted] prescription pharmaceutical products; release of Digoxin 0.125 mg lot #70924A2 following visual inspection of the [redacted] to remove "double thick tablets"; failure of the Quality Unit to reject products not meeting specifications, to complete Quality Assurance investigations, to expand investigations to other lots and products … and to respond to out of specification products on the marketplace. Analytical methods requiring remediation remained in use … . Written procedures were not followed and changes with potential product quality impact were not reviewed or approved by the Quality Unit. No market action was taken by the Quality Unit for any products on the market at the [March 18, 2008] initiation of the inspection despite the confirmed out of specification in-process, finished product, and stability results.

Pl. Ex. 91, (Bates 227); Pl. Ex. 500, (A37).

The FDA excoriates Actavis' inadequate quality control procedures, failure to follow those procedures, failure to reject out-of-specification product, failure to adequately review product to ensure it is within specification (whether or not it has been distributed), failure to investigate out-of-specification product in other production batches and products produced under the same systems and facilities, and failure to fully document investigation of out-of-specification product. Pl. Ex. 91, *generally*; Pl. Ex. 500, (A37).

The FDA concludes that but for a recall there simply could be no assurance of the strength, quality and purity of Actavis' products:

> Commitments to recall finished products from the marketplace were initiated on 4/9/08 and continued throughout the inspection for such products as Digoxin Tablets … . However, there is no assurance of the strength, quality and purity of the approximately [redacted] of other products that remain on the market, all lots remaining in the two distribution centers, and the in-process products … .

Pl. Ex. 91, (Bates 227); Pl. Ex. 500, (A37).

D. Digitek Recall: A little over a month after the start of the FDA inspection, Actavis finally acted upon its prior commitment to recall its defective products. Pl. Ex. 91, (Bates 227); Pl. Ex. 500, (A37). On April 24-25, 2008 (just one month too late for Mr. McCornack), Actavis instituted a nationwide recall of all Digitek.

The Digitek recall involved two full years of production (March 2006 - April 2008), 152 batches, and over five hundred million tablets. Pl. Ex. 113. One iteration of the recall notice, sent by Actavis to its "Valued Customers", provided:

> This recall notice has been initiated due to overweight tablets. Depending on the constituency of the tablets, double the dose size is taken, it can be expected that digitalis toxicity can occur in individuals taking daily doses or in patients with renal insufficiency. Toxicity can cause nausea, vomiting, dizziness, low blood pressure, cardiac instability and bradycardia. Death can result from excessive digitalis intake. If increased thickness is due to clinically inert substances, then a decreased amount of digitalis may be observed, leading to exacerbation of the underlying cardiac disease (congestive heart failure and arrhythmia) due to lack of therapeutic efficacy.

Pl. Ex. 113; Pl. Ex. 505, (Bates 1218); Pl. Ex. 120; Pl. Ex. 500, (A35, A57). Actavis' health hazard evaluation, the basis (nearly verbatim) for this notice, concluded that a double-dose ***of 0.125 mg Digitek*** would be expected to cause digoxin toxicity for daily-dose patients. Pl. Ex. 220.[3] Another iteration of the recall notice issued by Digitek's distributors (quoting Actavis' April 25, 2008 press release) provided:

> The voluntary recall is due to the possibility that tablets with double the appropriate thickness may have been commercially released. These tablets may contain twice the approved level of active ingredient than is appropriate.
>
> Digitek is used to treat heart failure and abnormal heart rhythms. The existence of double strength tablets poses a risk of digitalis toxicity in patients with renal failure. Digitalis toxicity can cause nausea, dizziness, low blood pressure, cardiac instability and bradycardia. Death can also result from excessive Digitalis intake.

Pl. Ex. 504, (Bates 1195, 1198-99, 1215-16).

The consumer-level recall notice mailed to Mr. McCornack by his pharmacy retailer dated May 2, 2008, less than two months after his death, similarly advised:

> On April 25, 2008, Actavis Totowa LLC, the manufacturer of Digitek 0.125 mg and Digitek 0.25 mg tablets, issued a Patient Level Recall of all lots of these products as a precaution **because the tablets may be double the appropriate thickness and could contain twice the approved level of active ingredient**. Because of this, the manufacturer is recalling all lots of these products.

Pl. Ex. 506, (Bates 1222, *emphasis in original*).

E. Mr. McCornack's Stable Medical History: Prior to his death on March 23, 2008, Mr. McCornack's medical condition was stable, with minimal risk of sudden cardiac death. He had taken digoxin (including Digitek) in conjunction with Diltiazam for more than a decade to minimize the discomfort of congenital, atrial fibrillation. His treatment had been without incident, and his regularly tested digoxin levels never exceeded the target, therapeutic range.

[3] The evaluation did not specifically address the more severe health hazards from taking a double-dose of 0.25 mg Digitek. Pl. Ex. 220.

Dr. Lawrence E. Von Dollen was Mr. McCornack's cardiologist for more than a decade. Pl. Ex. 600, (*Von Dollen Depo,* 95:1-5, 9:5-14). According to Dr. Von Dollen, Mr. McCornack's condition was stable, well-controlled by his medications, and did not place him at increased risk of sudden cardiac death. Dr. Von Dollen confirmed that the risk of sudden cardiac death was only minimally increased (if at all) by Mr. McCornack's atrial fibrillation. Pl. Ex. 600, (*Von Dollen Depo,* 43:7-44:4). His hypertension was considered "mild." *Id*., (44:5-23). He had no clinical indication of any arterial sclerotic heart disease, angina pectoris, or myocardial damage. *Id*., (44:24-45:7). Although perhaps carrying more weight than ideal, he was not obese. *Id*., (45:8-21). He lived an active lifestyle. *Id*., (72:12-23). He had no impairment in renal function. *Id*., (95:6-8). His condition was stable and it had not worsened over time. *Id*., (73:19-75:11). Symptomatically, he characterized Mr. McCornack's atrial fibrillation as predominantly a discomfort, with some negative impact on strenuous activity. *Id*., (47:7-16).

Dr. Gordon Lemm was Mr. McCornack's treating physician for 14 years and he co-managed Mr. McCornack's treatment with Dr. Von Dollen. Dr. Lemm has extensive experience treating cardiac issues (30% of his practice). Pl. Ex. 601, (*Lemm Depo,* 6:11-7:2, 8:10-9:4, 89:13-23). He examined Mr. McCornack in January, February, and March 2007 and there was no report or signs of any change in condition, or of any digoxin toxicity. *Id.*, (33:18-34:1).

Mr. McCornack had taken the same dose of Digitek and Diltiazam for years, without any incident or problems. Pl. Ex. 600, (*Von Dollen Depo*, 86:19-25); Pl. Ex. 601, (*Lemm Depo,* 65:6-9, 54:23-55:6). He was compliant about his medication regimen. Pl. Ex. 600, (*Von Dollen Depo*, 95:9-14, 57:17-60:5); Pl. Ex. 601, (*Lemm Depo*, 79:22-24, 90:12-17). *See also*, Pl. Ex. 602.1 and Pl. Ex. 609, (K. McCornack Depo, 60:9-61:13), (use of weekly pill organizer at time of death). Tested annually, including in May 2007, he always maintained a steady, consistent therapeutic

digoxin level of 1.4 -1.8 nanog/mL. Pl. Ex. 601, (*Lemm Depo*, 43:11-44:12, 54:23-55:6, 68:25-69:7, 90:4-11); Pl. Ex. 613, (Heard Depo, 44:20-41:2, test results ranged from 1.4 to 1.8, and never exceeded 2.0).

F. Mr. McCornack's Death: Just after midnight on March 23, 2008, on a family camping trip in the forests above Santa Cruz, a sleeping Mr. McCornack made an odd snoring noise which awoke his wife. She found him blue and non-responsive. He was pronounced dead by medics at 12:52 a.m. Earlier, he had complained to his wife of fatigue and gastrointestinal bloating. As normal, Mr. McCornack had taken his medications (including Digitek) at dinner time, 6:00-8:00 p.m. Pl. Ex. 602.1; Pl. Ex. 602.7 (Bates 10323); Pl. Ex. 609, (K. McCornack Depo, 51:12-52:6; 80:1-128:7; 106:15-25); Pl. Ex. 611, (R. McCornack Depo, 37:17-39:3); Pl. Ex. 610, (D. McCornack Depo, 68:11-15). At the time of his death, four-six hours after ingestion, Mr. McCornack was experiencing the peak effect of his Digitek. Pl. Ex. 607, (Gibson Report, Bates 11439, 11444).

Santa Cruz County Coroner, Dr. Richard T. Mason, performed the autopsy. Pl. Ex. 602, (*Mason Depo I*, 20:17-22:9). Following his normal procedures, he conducted a physical examination, collected blood and tissue samples for the lab, and dictated his initial report (subject to revision upon receipt of any aberrant lab results). *Id*., (12:9-13:5). A death certificate, based on this report, was issued April 7, 2008. Pl. Exs. 602.2, 602.3.

Dr. Mason originally ordered a standard therapeutic and abused drug blood screen (which did not include digoxin). Pl. Ex. 602.7, (Bates 10315); Pl. Ex. 602.5 (Bates 10289-91). Those results were returned on April 16, 2008. Pl. Ex. 602.5, (Bates 10289-91). In the interim, the Digitek recall occurred and review of Mr. McCornack's treating physicians' records continued, including an April 9 tabulation of Mr. McCornack's medications. *See, II.D supra*; Pl. Ex. 602.7,

(Bates 10325). On May 21, 2008, an additional test for digoxin was ordered. Pl. Ex. 602.7, (Bates 10319, post-it note). That result was returned on June 24, 2008 – a 3.6 nanog/mL digoxin level. Pl. Ex. 602.5, (Bates 10292-93). Dr. Mason amended the cause of death in the autopsy report to include digoxin toxicity. Pl. Ex. 509, (Mason Depo I, 18:1-19:21); Pl. Ex. 602.4; Pl. Ex. 602.5.[4] [5]

Every physician testifying (apart from defendants' retained witnesses) agrees that the 3.6 nanog/mL *post mortem* level is very significant, *post mortem* redistribution notwithstanding[6], and that digoxin toxicity was a cause of Mr. McCornack's death. *See, e.g.*, Pl. Ex. 602.5 (Autopsy Report); Pl. Ex. 603, (Mason Depo II) and Pl. Ex. 602, (Mason Depo I); Pl. Ex. 600, (Von Dollen Depo)[7]; Pl. Ex. 601, (*Lemm Depo*).[8] After consideration of Mr. McCornack's *post*

[4] To their extreme discredit, defendants try to sling mud against this ***veteran*** pathologist (*see*, Pl. Ex. 509.6; Pl. Ex. 602, (Mason Depo I, 9:8-10:22)) questioning his amendment of the autopsy report on the day prior to his first deposition. Dr. Mason confirms, however, that amendment based on subsequently received lab results is standard procedure and commonplace (id., 12:9-13:5), and that he had meant to amend his diagnosis for some time (long before any involvement in this litigation) but for a backlog of other work (id., 33:11-22).

[5] Defendants' forensic pathologist expert (Dr. McMaster) confirms that Dr. Mason was correct to reconsider his diagnosis of cause of death after learning of the Digitek recall and *post mortem* digoxin level. Although reaching a different conclusion, she confirms that his methods were the same methods she would have used. Pl. Ex. 604, (McMaster Depo, 11:12-17, 12:9-18, 13:3-6, 58:19-60:9, 63:12-64:1, 65:19-23, 69:24-70:11, 86:22-87:9, 87:20-88:7, 97:12-16) and see Pl. Ex. 605, (McMaster Expert Report, reflecting same basic method).

[6] *Post mortem* redistribution is the transfer of drugs after death from areas of high concentration to areas of low concentration, in this case primarily from the myocardium into the blood. Pl. Ex. 607, (Gibson Expert Report, Bates 11441-43). Where this occurs, *post mortem* blood levels exceed the *ante mortem* levels.

[7] Dr. Von Dollen has diagnosed dozens of patients with digoxin toxicity during his career, including 5-10 presenting emergency room situations. Pl. Ex. 600, (Von Dollen Depo, 31:8-18). Based on Mr. McCornack's *post mortem* digoxin level and the absence of another adequate explanation for his death, Dr. Von Dollen opined that to a reasonable medical probability digoxin toxicity was a cause of death. *Id.*, 82:20-85:16, 95:22-96:4 (death consistent with digoxin toxicity), 96:6-97:13, (more likely than not digoxin toxicity was cause of death).

mortem digoxin level, the Vorpahl Study (*see below*), the Digitek recall for excessive dose product, the events of the date of death (including the medication regimen), and the treating physicians' records, Dr. Mason reaffirmed his opinion that Mr. McCornack died of "[c]cardiac arrest due to ventricular arrhythmia due to digoxin toxicity due to digoxin poisoning." Pl. Ex. 603, (Mason Depo II, 156:20-164:11). Redistribution notwithstanding, the 3.6 ng/mL test result remained sufficiently elevated to support amendment of his diagnosis given that peripheral blood had been sampled and the corpse had been properly refrigerated and undisturbed. Pl. Ex. 602, (Mason Depo I, 54:9-56:9). This elevated digoxin level is significant in view of Mr. McCornack's long-standing stable condition, stable therapeutic digoxin levels, and the absence of evidence of another likely cause. *See, II.E. supra, and fn. 9-11*.[9]

Defendants' experts do not take issue with the accuracy of the 3.6 ng/mL *post mortem* test result. Pl. Ex. 608, (Brown Depo, 89:1-16) and Pl. Ex. 604, (McMaster Depo, 32:14-33:5).

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[8] Dr. Lemm has previously diagnosed patients with digoxin toxicity on about ten occasions. Pl. Ex. 601, (Lemm Depo, 26:21-27:7). He was immediately "very suspicious" that digoxin toxicity had caused Mr. McCornack's death, in light of the Digitek recall and the absence of indicia of another cause. *Id*., 22:18-23:7, 23:11-24:14, 26:21-27:7). His suspicions were heightened when he learned of the 3.6 nanog/mL result. *Id*., (54:12-22, 70:3-11, 70:25-71:16), ("a patient getting over about 2.4, I'd be really concerned of toxicity"; "I would be really concerned that this was a toxic level ... looking at that 3.6 level"; "I'm not an expert in that [post mortem redistribution]. I still would be worried, though, with a 3.6. Definitely throw up a red flag."). After consideration of all the various relevant factors, including the potential impact of *post mortem* redistribution, Dr. Lemm confirmed that his opinion remained unchanged – Mr. McCornack had received an excessive dose of digoxin and digoxin toxicity led to his death. *Id*., (54:23-55:6, 89:13-92:6).

[9] Defendants have argued that an elevated *post mortem* Diltiazam level may be an alternate cause of death. Their own expert (Dr. Galanter), however, does not believe Diltiazam played any part in causing the death. Pl. Ex. 612, (Galanter Depo, 31:19-22). *See also*, Pl. Ex. 600, (Von Dollen Depo, 86:1-18, 52:13-21, 87:1-21, no concern re Diltiazam toxicity; Diltiazam toxicity not an issue at the prescribed dosage). A far less dangerous drug than Digitek, Diltiazam typically presents a risk of death at *post mortem* levels of 6,700-33,000 nanog/mL, with a mean of 16,000 nanog/mL. Pl. Ex. 602.7, (Bates 10310). Mr. McCornack's *post mortem* test result of 630 nanog/mL does not approach such a level. *Id*., (Bates 10309)

Instead, defendants hope to simply discard it as an unreliable indicator of *ante mortem* levels due to the effects of *post mortem* redistribution (*see fn. 8 supra*). But at least one defense expert (Dr. Heard) concedes that redistribution notwithstanding, the 3.6 ng/mL *post mortem* result is consistent with an excessive dose of digoxin. Pl. Ex. 613, (Heard Depo, 69:18-70:14, 3.6 ng/mL *post mortem* result consistent with an excessive dose; 40:24-41:13, 3.6 nanog/mL *post mortem* result may indicate *ante mortem* level "well above 2.0"). Defense pathologist Dr. McMaster confirms that she routinely uses *post mortem* levels to opine on *ante mortem* levels, and that it is entirely appropriate and important for a forensic pathologist to do so. Pl. Ex. 604, (McMaster Depo, 11:12-17, 12:9-18, 13:3-6, 43:23-45:4, 58:19-60:9, 63:12-64:1, 65:19-23, 69:24-70:11, 86:22-87:9, 97:12-16); Pl. Ex. 605, (McMaster Report citing the Vorpahl Study, *see below*).

The significance of the 3.6 nanog/mL lab result is supported by the seminal Vorphal & Coe Study, *Correlation of Antemortem and Postmortem Digoxin Levels* ("Vorpahl Study") which found that the mean ratio between *post* and *ante mortem* digoxin levels, for peripheral blood samples, is 1.42. Pl. Ex. 601.2, (Bates 10104). The Vorpahl Study's digoxin redistribution ratio is in turn cited in Baselt's well-respected toxicology treatise, *Disposition of Toxic Drugs and Chemicals in Man*. Pl. Ex. 602.9 (Bates 10355). Both were considered by Dr. Mason. Pl. Ex. 602, (Mason Depo I, 36:7-8, 44:12- 45:22); Pl. Ex. 602.9; Pl. Ex. 603, (Mason Depo II, 158:20-165:11); Pl. Ex. 603.16.

Applying the Vorpahl Study's ratio, Mr. McCornack's calculated *ante mortem* digoxin blood level is 2.5 nanog/ mL, exceeding accepted therapeutic levels. A significant potential for digoxin toxicity arises at levels in excess of 2.0. Pl. Ex. 600, (*Von Dollen Depo*, 29:21-30:8, 88:7-9, tries to hold patients below 2.0; 31:8-34:11, potential for toxicity above 2.0); Pl. Ex. 601, (*Lemm Depo*, 41:8-42:8, target therapeutic range between 1.0 and 2.0; 54:12-22, "really

concerned about toxicity" above 2.4); Pl. Ex. 602, (Mason Depo I, 40:3-41:13). Defendants' experts concur. Pl. Ex. 613, (*Heard Depo*, 12:25-13:4, level above 2.0 is abnormal); Pl. Ex. 608, (*Brown Depo*, 32:14-16, 37:5-13, 38:1-3, "possibility the patient may have signs of toxicity" above 2.0). Perhaps more instructive, the calculated 2.5 nanog/mL level significantly exceeds Mr. McCornack's longstanding 1.4-1.8 nanog/mL annual test levels. *See citations supra*.

Generally, defendants' experts do not take issue with Vorpahl or Baselt.[10] Instead, they argue that the Vorpahl Study's ratio is inapplicable to calculate redistribution here, where the blood sample was collected 79 hours after the time of death (a reality of a Coroner's practice), (whereas the Vorpahl Study sampling occurred within 10 hours).[11] Defendants' experts concede, however, that there is no actual study of whether this would materially change the Vorpahl Study ratio, (Pl. Ex. 613, (Heard Depo, 41:6-12); Pl. Ex. 608, (Brown Depo, 60:10-17), particularly where (as here) the body has been kept refrigerated and undisturbed in the Coroner's custody. In Dr. Mason's opinion, peripheral sampling and such proper handling of the remains slows decomposition (and redistribution), such that the time of sampling would not be significant. Pl. Ex. 602, (Mason Depo I, 42:6-43:6; 46:8-47:1).

Finally, while defendants' experts may disagree about cause of death, they at least concur that the manner of death was consistent with digoxin toxicity, both from a pathological and a

[10] Pl. Ex. 605 (McMaster Expert Report, quoting Baselt for the Vorpahl Study's redistribution ratio analysis); Pl. Ex. 604, (McMaster Depo, 43:23-45:4); Pl. Ex. 612, (*Galanter Depo*, 10:4-12, conceding Vorpahl Study properly reflects the patient population studied, but disagreeing with the "scope of generalities; 47:17-48:1, 48:23-49:6, 50:12-24, 51:2-11, 135:20-136:1, conceding there are studies concluding *post mortem* results can predict *ante mortem* levels and properly inform a diagnosis of digoxin toxicity), Pl. Ex. 612.1, (Galanter Expert Report, No. 15, relying on a clinical report which used *post mortem* results to predict *ante mortem* levels).

[11] Defendants have also attempted to distinguish the Vorpahl Study by arguing that Dr. Mason did not collect a peripheral blood sample. This is inaccurate. Pl. Ex. 602, (Mason Depo I, 23:16-25:6, 25:24-27:8, blood collected from peripheral axillary veins); Pl. Ex. 608, (Brown Depo, 89:24-90:21, axillary blood is considered peripheral blood).

clinical perspective. Clinical symptoms of digoxin toxicity may include dizziness, light-headedness, slower pulse, shortness of breath, tiredness, fatigue, lack of energy, nausea, lethargy, or vision issues. Pl. Ex. 600, (Von Dollen Depo, 28:7-29:20, 33:19-34:11); Pl. Ex. 601, (Lemm Depo, 32:20-25); Pl. Ex. 607, (Gibson Expert Report, Bates 11440). Sometimes, symptoms are mild enough to sleep through; sometimes, there are no symptoms at all prior to sudden cardiac death. Pl. Ex. 600, (Von Dollen, 92:17-93:13); Pl. Ex. 613, (Heard Depo, 76:23-77:1); Pl. Ex. 608, (Brown Depo, 74:17-21). Mr. McCornack's report of fatigue and gastrointestinal bloating before his sudden cardiac death (*see II.E supra*) is clinically consistent with digoxin toxicity. Pl. Ex. 613, (Heard Depo, 19:4-20, 38:1-9, 40:13-23, 57:21-58:23, fatigue and bloating clinically consistent with digoxin toxicity).

Pathologically, Mr. McCornack's ventricular arrhythmia and sudden cardiac death are likewise conceded to be consistent with digoxin toxicity. Pl. Ex. 613. (Heard Depo, 19:4-20, 38:1-9, 40:13-23, 57:21-58:23, sudden cardiac death and ventricular tachycardia consistent with digoxin toxicity); Pl. Ex. 612, (Galanter Depo, 53:6-8, 64:20-65:22, 90:17-91:9, sudden cardiac death consistent with digoxin toxicity); Pl. Ex. 608, (Brown Depo, 86:22-24, elevated digoxin blood level can cause ventricular arrhythmia); Pl. Ex. 604, (McMaster Depo, 55:15-22, sudden cardiac death consistent with digoxin toxicity).

III. ARGUMENT

Defendants' Motion for Summary Judgment asserts there is no evidence that any Plaintiff suffered an injury caused by a defective dose of digoxin. Defendants are simply wrong and the preceding Statement of Facts should make that abundantly clear. Plaintiffs' quality control expert states that more likely than not defective tablets were released to consumers based on the lack of quality controls at the Actavis factory and evidenced by numerous instances of defective

tablets being produced and released from the Actavis facility. Further, both of Mr. McCornack's treating physicians Lemm and Von Dollen together with the pathologist Dr. Mason that performed the autopsy all agreed that more likely than not, Mr. McCornack died due to digoxin toxicity as evidenced by a high post-mortem digoxin blood level, a cardiac arrest consistent with digoxin toxicity, several pre-death clinical symptoms consistent with digoxin toxicity, and the absence of any other likely cause of death. Among other things, the treating physicians, a pharmacist Dr. keith Gibson, and other witnesses explain that there is no evidence that anything other than a defective tablets could have caused Mr. McCornack's digoxin toxicity because Mr. McCornack was in a state of good health prior to his cardiac arrest, he had been stable on his medication for over 10 years, he was consistent and compliant in following his prescription, he was using a pill organizer on the day he died, which made the possibility of double dosing extremely unlikely, and there was no other medical explanation for digoxin toxicity other than a defective tablet. For all of these reasons, a genuine issue of material fact exists that Mr. McCornack died because he consumed defective Digitek tablets that contained twice the normal level of digoxin. Therefore, Defendants' Motion for Summary Judgment must be denied.

A. Burden of Proof

1. The Court Should Shift The Burden of Proof Of Causation.

"[W]hen there is a substantial probability that a defendant's negligence makes it impossible, as a practical matter, for plaintiff to prove 'proximate causation' conclusively, it is more appropriate to hold the defendant liable than to deny an innocent plaintiff recovery, unless the defendant can proved that his negligence was not a cause of the injury." *Haft v. Lone Palm Hotel*, 3 Cal.3d 756, 774, fn. 19 (1970). Defendants' ignore the fact that at least for Mr. McCornack and Mrs. Vega, that they may have consumed one or more, or perhaps the only

defective tablets in their possession and that it was Defendants' negligence that was responsible for that. Defendants failed to conduct an inspection of all of the tablets released using a qualified method. For example, in Batch 70924A1, Defendants found only 20 tablets out of approximately 4.7 million tablets in the batch. While obviously the ratio of defective tablets to non-defective tablets will be small, it is disingenuous for Defendants to argue that Plaintiffs should have been able to locate a defective tablet given that each plaintiff had a maximum of perhaps 30-100 tablets in their possession at any one time. The defendants recalled 152 batches representing over 700 million tablets. The odds of locating a second defective pill (apart from the one ingested) are not a needle in a haystack, they are a needle in a 10,000 acre hayfield. Because Defendants' negligence has made proof of causation unreasonably difficult, the Court should shift the burden of proof to the Defendants to prove their negligence was not a cause of Mr. McCornack's death.

2. Even If The Court Does Not Shift The Burden Of Proof, Plaintiff Only Need Establish A Genuine Issue Of Material Fact To Defeat Summary Judgment.

When the nonmoving party will bear the burden of proof on a dispositive issue at trial, the court must deny the moving party's motion for summary judgment if there are "specific facts showing that there is a genuine issue for trial." *Celotex Corp. v. Catrett,* 477 U.S. 317, 323-324 (1986). A genuine issue of material fact exists if, in viewing the record and all reasonable inferences drawn therefrom in a light most favorable to the non-moving party, a reasonable juror could return a verdict for the non-movant. *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 248 (1986). The test is whether the evidence opposing the Motion is such that it could cause *reasonable persons to disagree* on whether the facts claimed by the opposing party are true enough to require a jury to resolve the differing versions of the truth. *Aydin Corp. v. Loral*

Corp., 718 F.2d 897, 902 (9th Cir. 1983). The party opposing the summary judgment is entitled to have their version of the facts accepted as true and, moreover, to have all internal conflicts resolved in their favor. *Charbonnages de France v. Smith,* 597 F.2d 406, 414 (4th Cir. 1979). Likewise, inferences that are drawn from the underlying facts "must be viewed in the light most favorable to the party opposing the motion." *United States v. Diebold, Inc.*, 369 U.S. 654, 655 (1962). And finally, while the *facts* on which the opponent relies must be admissible at trial, they need not be in an admissible *form* as presented in the opposition. *Celotex Corp. v. Catrett,* 477 U.S. at 324. 323. Among other things, expert opinion will raise a triable issue of fact so long as the expert is competent to give an opinion and the factual basis for the opinion is disclosed. *Triton Energy Corp. v. Square D. Co.*, 68 F.3d 1216, 1222 (9th Cir. 1995).

Here, Plaintiffs' ultimate burden at trial will be to show that a digitek tablet was defective and that the defect caused Mr. McCornack's death. *Grinnell v. Pfizer & Co.*, 274 Cal.App.2d 424, 435, 79 Cal.Rptr. 369 (1969). Expert opinion will raise a triable issue of fact so long as the expert is competent to give an opinion and the factual basis for the opinion is disclosed. *Triton Energy Corp. v. Square D. Co.*, 68 F.3d 1216, 1222 (9th Cir. 1995). Such proof need not be definitive and at the summary judgment stage all that is required is that Plaintiffs introduce evidence that affords a reasonable basis for the conclusion that is more likely than not that the conduct of Defendants was a substantial factor in causing Mr. McCornack's death. *Aydin Corp. v. Loral Corp.*, 718 F.2d 897, 902 (9th Cir. 1983); *Grinnell v. Pfizer & Co.*, 274 Cal.App.2d at 435. For example, in *Grinnell*, the court held that substantial circumstantial evidence existed from which a jury could infer that defendant's oral polio vaccine was the cause of polio suffered by plaintiffs, and the jury was also entitled to infer from the evidence that if the vaccine caused the polio, it was defective. The same situation is presented here. The evidence from Plaintiffs

medical experts and other documentary evidence lead to the conclusion that Mr. McCornack died of digoxin poisoning. The evidence is circumstantial, but a jury can infer from the evidence presented here that the Digitek taken by Mr. McCornack was out of specification and caused his death. Because the tablet taken by Mr. McCornak on the day he died was ingested and consumed, there will never be direct evidence that that tablet's potency, size or weight. Circumstantial evidence must be used, and the Plaintiffs have presented an overwhelming body of circumstantial evidence that will entitle a jury to infer that Mr. McCornack took out- of-specification and defective Digitek that caused his death.

B. Plaintiffs' Evidence Creates Genuine Issues Of Material Facts.

1. Defective Tablets Were Released To The Public.

Plaintiffs' quality control experts have reviewed the documents in this case and examined the Quality System at the Actavis Little Falls production plant and concluded that more likely than not double strength and out-of-specification digoxin tablets were released to consumers. (Bliesner Dec.Exh.620; Pl.Exh.500 at p.663[Bliesner Report]; and Farley Depo.450:24 to 454:4.)

Defendants' arguments to the contrary are inaccurate and misleading based upon the defendant's own records. (See Section II(B) above and Pl. Exs. 128 and 242 (double thick tablet); Pl. Ex. M69 at p. 660 (multiple complaints (undersized tablet); Defense Ex. 527.1 ("obviously" double thick tablet) Pl. Ex. 73, p. 109 (nine complaints of double-thick tablets).)

Defendants are wrong again when they assert that violation of the CGMPs are not circumstantial evidence that an out-of-specification tablet was released to the public. Documented GMP violations in this case relate to tablets *actually* being manufactured out-of-specification – i.e. blend failures, super and sub-potent tablets, thick and thin tablets, etc. (See Section II(B) and (C) above.) The Defendants' failure to follow qualified GMPs after

discovering these manufacturing defects (i.e. a "visual inspection" of 4.8 million tablets) means there was no way for Defendants to know if they located all defective tablets in a batch before releasing them. (Pl. Ex. 500, 511, 514, 516.) The jury is entitled to make an inference from the fact that the Defendants did not follow CGMPs, and that Defendants' "investigation" procedures were inadequate making it more likely than not that defective tablets were released to the public. This is significant and probative circumstantial evidence of the manufacturing defect at issue in this case.

Defendants also incorrectly argue that violations of FDA regulations do not constitute proof of a defect. (Def. Motion at p. 8.) The cases cited by Defendants only stand for the proposition that proof of a recall alone does not prove a defect. But the circumstantial evidence of a recall is admissible and relevant evidence upon which a jury may rely in reaching its decision. *Longenecker v. G.M. Corp.*, 594 F.2d 1283, 1286 (9th Cir. 1979); see also *Webster v. Body Dynamics, Inc.*, 27 So.3d 805, fn. 10 (2010) [citing state and federal cases admitting recall letters]. The Defendants attempt to isolate each piece of evidence in this case and claim that the evidence, standing alone, is inadequate

2. <u>Dan McCornack Died By Consuming A Defective Tablet Of Digoxin.</u>

There is no requirement that the McCornack family produce a defect tablet to prevail on this summary judgment motion. Instead, under California law (and most other jurisdictions) a prima facie case may be proved by circumstantial evidence of a malfunction of a product. *Hinkley v. La Mesa R.V. Center, Inc.*, 158 Cal.App.3d 630, 643 (1984) [a product defect may be inferred if the facts tend to show the defect existed before the accident. - citing Prosser, Law of Torts, (4th Ed. 1971) Products Liability, Proof, section 103 at p. 673]; *Notmeyer v. Stryker Corp.*, 502 F.Supp.2d 1051 (N.D. Cal. 2007) [same]. The medical and other witnesses explained that

there is no compelling evidence that anything other than a defective tablets would likely have caused Mr. McCornack's digoxin toxicity because Mr. McCornack was in a state of good health prior to his cardiac arrest, he had been stable on his medication for over 10 years, he was consistent and compliant in following his prescription, he was using a pill organizer on the day he died (which made the possibility of double dosing extremely unlikely), and there was no other medical explanation for digoxin toxicity other than a defective tablet. The motion should be denied.

C. Violation of Local Rule 7.1

Defendant's motion should be denied because it violates LR Civ P 7.1. The motion incorporates and repeatedly refers to the 20 page argument contained in the separately filed general background statement, making the motion essentially 40 pages in length.

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/s/ Don A. Ernst
Don A. Ernst (CA State Bar No. 065726)
Attorneys for Plaintiffs
Ernst Law Group
1020 Palm Street
San Luis Obispo, CA 93401
Tel: 805-541-0300
Fax: 805-541-5168
E-mail: de@ernstlawgroup.com